

Claims

1. Compounds of the general formula (I) – wherein R means
- 5 - a nitrogen-containing one- or two-ring aromatic moiety consisting of one or two aromatic rings, preferably pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl rings which is
- 10 in a given case independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl group, C1-4 alkoxy group, halogen atom, trihalogenomethyl group, methylthio group, nitro group, cyano group, C2-5 alkoxycarbonyl groups or carboxamido group; or
- p-tolylsulfonyl group; or
- 15 - R_{1a} -CH₂-group, where the meaning of R_{1a} is hydrogen, C1-4 alkyl group, phenyl, benzyl, phenylethyl, phenylethenyl, naphthyl, pyridyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, thienyl, furyl or p-tolylsulfonyl moieties which are substituted in a given case independently from each other by one or more C1-4 alkyl, C1-4 alkoxy, alkylenedioxy group, halogen atom, trihalogenomethyl, nitro or cyano
- 20 group; or
- R_{1b} -CO-group, where the meaning of R_{1b} is C1-4 alkyl group, phenyl, benzyl, phenylethyl, phenylethenyl, naphthyl, pyridyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl or quinoxalinyl moieties optionally substituted independently from each other by one or more C1-4 alkyl groups, C1-4 alkoxy groups, alkylenedioxy
- 25 groups, halogen atom, trihalogenomethyl, nitro or cyano group; mono- or disubstituted

amino group, saturated N-containing heterocyclic moiety, preferably a group containing pyrrolidino, piperidino, piperazino or morpholino ring;

B stands for a group according to the formula (1) or (2) or (3) or (4);

Z stands for a groups of formula (A) or (B) or (C) or (D) or (E) or (F);

5 and the salts, isomers, tautomers, hydrates or solvates thereof.

2. Compounds of the general formula (I) as defined in claim 1 – wherein R means

- a nitrogen-containing one- or two-ring aromatic moiety consisting of one or two aromatic rings, preferably pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, imidazolyl, pirazolyl, 10 thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, quinoliny, isoquinoliny, cinnoliny, phthalazinyl, quinazolinyl, quinoxaliny, benzimidazolyl, indazolyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl or benzisoxazolyl rings which is in a given case independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl group, C1-4 alkoxy group, halogen atom, trihalogenomethyl group, 15 methylthio group, nitro group, cyano group; or

- p-tolylsulfonyl group; or

- R_{1a} -CH₂-group, where the meaning of R_{1a} is hydrogen, C1-4 alkyl group, phenyl, benzyl, phenylethyl, phenylethenyl, naphthyl, pyridyl, quinolyl, isoquinolyl, cinnoliny, phthalazinyl, quinazolinyl, quinoxaliny, thienyl, furyl or p-tolylsulfonyl moieties which 20 are substituted in a given case independently from each other by one or more C1-4 alkyl, C1-4 alkoxy, alkylenedioxy group, halogen atom, trihalogenomethyl, nitro or cyano group; or

- R_{1b} -CO-group, where the meaning of R_{1b} is C1-4 alkyl group, phenyl, benzyl, phenylethyl, phenylethenyl, naphthyl, pyridyl, quinolyl, isoquinolyl, cinnoliny, 25 phthalazinyl, quinazolinyl or quinoxaliny moieties optionally substituted independently from each other by one or more C1-4 alkyl groups, C1-4 alkoxy groups, alkylenedioxy

groups, halogen atom, trihalogenomethyl, nitro or cyano group; mono- or disubstituted amino group, saturated N-containing heterocyclic moiety, preferably a group containing pyrrolidino, piperidino, piperazino or morpholino ring;

B stands for a group according to the formula (1) or (2) or (3) or (4);

5 Z stands for a groups of formula (A) or (B) or (C) or (D) or (E) or (F);

and the salts, isomers, tautomers, hydrates or solvates thereof.

3. Compounds of the general formula (I) as defined in claim 1 - wherein

- R means pyrimidinyl-, pyridinyl-, pyrazinyl-, pyridazinyl-, benzothiazolyl-,
10 benzisothiazolyl-, benzoxazolyl-, benzisoxazolyl-group which is in a given case independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl group, C1-4 alkoxy group, halogen atom, nitro group, cyano group, C2-5 alkoxy carbonyl group or carboxamido group; or
p-tolylsulfonyl-group; or

15 R_{1a} - CH₂-group wherein the meaning of R_{1a} is benzyl group or phenylethenyl group substituted in a give case independently by one or more C1-4 alkyl pr alkylene dioxy group; or

R_{1b}CO group where the meaning of R_{1b} is phenyl, benzyl, phenylethyl, phenylethenyl or
pyperidino group which is in a given case substituted independently from each other by
20 alkylendioxy group;

B stands for a group of the formula (1) or (2) or (3) or (4) ;

Z stands for a group of formula (A) or formula (B) ; - and the salts, isomers, tautomers, hydrates or solvates thereof.

25 4. Compounds of the general formula (I) as defined in claim 1 - wherein

- R means pyrimidinyl-, pyridinyl-, pyrazinyl-, pyridazinyl-, benzothiazolyl-, benzisothiazolyl-, benzoxazolyl-, benzisoxazolyl-group which is in a given case independently from each other mono- or disubstituted by one or two of the following groups: C1-4 alkyl group, C1-4 alkoxy group, halogen atom, nitro group, cyano group; or
5 p-tolylsulfonyl-group; or

R_{1a} - CH₂-group wherein the meaning of R_{1a} is benzyl group or phenylethenyl group substituted in a give case independently by one or more C1-4 alkyl pr alkylene dioxy group; or

R_{1b}CO group where the meaning of R_{1b} is phenyl, benzyl, phenylethyl, phenylethenyl or
10 piperidino group which is in a given case substituted independently from each other by alkylenedioxy group;

B stands for a group of the formula (1) or (2) or (3) or (4) ;

Z stands for a group of formula (A) or formula (B) ; - and the salts, isomers, tautomers, hydrates or solvates thereof.

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5. Compounds of the general formula (I) as defined in claim 1 – wherein R means a pyrimidyl or pyridyl or pyrazinyl group substituted with nitro or cyano group, B means a groups of formula (1) or (2), and Z means a group of formula (A) or (B) – as well as their salts, isomers, tautomers, hydrates or solvates.

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6. (4*R*)-3-(2-{{[8-(2-Pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]}*exo*-amino}acetyl)thiazolidine-4-carbonitrile;

7. (4*R*)-3-(2-{{[8-(5-Cyanopyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]}*exo*-amino}acetyl)thiazolidine-4-carbonitrile;

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8. (4*R*)-3-(2-{{[8-(5-Cyanopyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]-endo-amino}acetyl}thiazolidine-4-carbonitrile;
9. (4*R*)-3-(2-{{[8-(2-Pyrazinyl)-8-azabicyclo[3.2.1]octan-3-yl]-exo-amino}acetyl}thiazolidine-4-carbonitrile;
10. (2*S*)-1-(2-{{[8-(5-Nitropyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl]-exo-amino}acetyl}pyrrolidine-2-carbonitrile;
11. Pharmaceutical composition characterized by containing a compound of the general formula (I) - wherein the meanings of R, B and Z are the same as defined in Claim 1 - or isomers or solvates thereof, in the form of the free compound or of a salt, and at least one pharmaceutically accepted support material or diluents.
12. Process for the preparation of the compounds of the general formula (I) - wherein the meanings of R, B and Z are the same as defined in Claim 1 - characterized by reacting a compound of the general formula (II) - wherein the meaning of R is as defined above - with a compound of the general formula (III) - wherein the meaning Z is as defined above - and isolating the resulting compound of the general formula (I) or its salt from the reaction mixture.
13. Use of a compound of the general formula (I) - wherein the meanings of R, B and Z are as defined in Claim 1 - for the preparation of pharmaceutical compositions suitable to inhibit DPP-IV enzyme activity, thus suitable to treat diseases related with DPP-IV enzyme concentration.

14. Process for inhibition of the DPP-IV enzyme and for treatment of diseases related with the DPP-IV enzyme concentration, characterized in that a compound of the general formula (I) as defined in Claim 1 is applied in therapeutically effective amount, in the form of the free compound, or of a salt.

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15. Compounds of the general formula (II) – wherein the meanings of R and B are as defined in claim 1 – and their salts.

16. Compounds of the general formula (V) – wherein the meaning of R is as defined in
10 claim 1 and Y means *tert*-butoxycarbonyl group.

17. Compounds of the general formula (VII) – wherein the meaning of Z is as defined in claim 1.

15 18. Compounds of the general formula (VIII) – wherein the meaning of Z is as defined in claim 1 - and their salts.

19. Compounds of the general formula (IX) – wherein the meaning of Z is as defined in claim 1.

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20. Compounds of the general formula (III) – wherein the meaning of Z is as defined in claim 1.